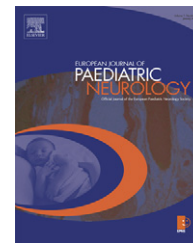




Official Journal of the European Paediatric Neurology Society



Case study

From juvenile parkinsonism to encephalitis lethargica, a new phenotype of post-streptococcal disorders: Case report

Pedro Beleza^{a,*}, João Soares-Fernandes^b, Maria J. Jordão^a, Fátima Almeida^a

^aDepartment of Neurology, Hospital São Marcos, Largo Carlos Amarante, Apartado 2242, 4701-965 Braga, Portugal

^bDepartment of Neuroradiology, São Marcos Hospital, Braga, Portugal

ARTICLE INFO

Article history:

Received 31 July 2007

Received in revised form

29 November 2007

Accepted 30 November 2007

Keywords:

Post-streptococcal disorder

Encephalitis lethargica

Parkinsonism

ABSTRACT

We report the case of a 16-year-old boy presented with a mild akinetic-rigid parkinsonism shortly after a post-streptococcal infection. After stopping corticoids, he had a rapid neurological deterioration to a fatal encephalitis lethargica-like syndrome. Serum analysis demonstrated consistently elevated anti-streptolysin-O. This case illustrates a new severe phenotype in the spectrum of the post-streptococcal disorders. This etiology should be considered in the differential diagnosis of a movement disorder with a rapid detrimental evolution.

© 2007 European Paediatric Neurology Society. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Group A streptococcal infection is associated with autoimmune neuropsychiatric symptoms, typically with a relapsing-remitting course, possibly mediated by antibodies against basal ganglia neurons.¹

We describe a boy who presented a mild parkinsonism and who after stopping corticoids had a dramatic evolution to an akinetic-mutism state associated with an inflammatory CSF and widespread brain lesions. Although ds-DNA was mildly positive, the diagnosis of systemic lupus erythematosus was considered less probable inasmuch as the antinuclear and anti-ENA antibodies were negative, complement levels were normal and no other clinical or laboratorial criteria was present.

2. Case report

A 16-year-old right-handed boy presented with left akinetic-rigid parkinsonism 2 weeks after complete recovery of an episode of pharyngitis. His medical history was remarkable for bilateral knee arthralgias, recurrent amygdalitis and increased ASO titers since 9 years of age.

The imaging and laboratory study, performed 2 months after the clinical onset, was normal except for the finding of high ASO titers (245 µL/mL; normal <200 µL/mL). The work-up included brain CT and MRI, hemogram, renal, hepatic and thyroid functions, urinary and serum copper, ceruloplasmin, erythrocyte sedimentation rate (ESR), ANA, ANCA, lupus anticoagulant, anticardiolipin antibodies, circulant immuno-complexes and urinary sediment.

*Corresponding author. Tel.: +351 253209000.

E-mail address: beleza.76@gmail.com (P. Beleza).

During the first 6 months, he presented a stabilized course, showing mild clinical improvement after trihexifenidil 2 mg tid and also when piribedil 50 mg tid was added.

Afterwards, he presented a progressive clinical deterioration, with increasing rigidity and bradykinesia predominantly in the left limbs. He was then provided levodopa/carbidopa 25/100 mg tid and hydrocortisone 150 mg IV on alternate days replacing the previous drugs. This resulted in a clear clinical improvement. He took hydrocortisone for 24 days. Four days after stopping it, and despite still taking levodopa/carbidopa 25/100 mg tid, he presented a rapidly progressive neurological deterioration consisting of auditory allucinations, speech and gait slowness and frequent falls. He progressed within 6 days to an akinetic-mutism state with somnolence, generalized limb and nuchal rigidity, left limbs dystonia and hyperthermia as was seen on the day he was admitted in the Emergency Room (ER).

In the blood study, we underline hemoglobin of 8.9 g/dL with a normal peripheral smear and negative Combs test. ESR was increased (112 mm/h; normal <20 mm/h) as was creatinine kinase (CK) (810 IU/L; normal 40–175 IU/L), and C-reactive protein (CRP) was normal. CSF study revealed 60 cells/ μ L (85% lymphocytes), 0.51 g/dL proteins, normal glycorraquia and negative viruses PCR for Measles, Herpes Simplex, Varicella Zoster, Herpes 6, CMV, EBV and Enterovirus. Serum (Measles, VDRL, HIV, HBV, HCV, CMV, EBV), metabolic (lactate, pyruvate

and molecular study) and microbiological studies in the CSF and blood were all negatives. Immunological study showed high ASO titer of 1280 μ L/mL on day 4 and 1300 μ L/mL on day 11 showing the consistency of the finding. Hep-2 ANA, Anti Sm, Anti-RNP, Anti-SSA, Anti-SSB, C3, C4, CH50 and immune complexes were all normal or negative and ELISA ds-DNA, 42.1 μ L/min (normal <5 mg/mL). Brain CT and MRI showed extensive lesions, involving cortical and subcortical regions bilaterally, left insula and putamen (Fig. 1A and B). EEG showed a theta stupor (5 Hz) without periodic activity.

He was then treated with methylprednisolone 1 g IV id for 5 days, acyclovir 10 mg/kg IV q8h for 14 days, cefotaxime 2 g IV q4h for 12 days and levodopa/carbidopa up to 125 mg tid. During the first 2 weeks, he showed no clinical improvement, keeping the hyperthermia. On day 33, his neurological condition worsened presenting brainstem dysfunction signs and CT scan showed bilateral hypodensity and brain edema (Fig. 1C and D). Then methylprednisolone cycle combined with cyclophosphamide was initiated. However, unfortunately he died 2 days later.

3. Discussion

We describe a 16-year-old-boy who developed a progressive neurological disease following a pharyngitis. Starting with an assymetric parkinsonism, he had a catastrophic evolution after corticoid suspension. This suggested the inflammatory nature of the disease which was further corroborated by the laboratory data. Actually, the blood investigation disclosed high ESR level with normal PCR and the infectious and metabolic studies performed on CSF and blood were all normal.

His past medical history of bilateral arthralgias, the occurrence of neurological deterioration with psychosis and the high serum ds-DNA raised the hypothesis of systemic lupus erythematosus (SLE). Children with SLE have a more severe disease onset than adults² and fever is a common early manifestation.³ In fact, juvenile parkinsonism (mainly the rigid-akinetic form), despite rare and not included in the 19 neuropsychiatric syndromes defined by the American College of the Rheumatology (ACR),⁴ is a known manifestation of SLE.⁵ In our patient, however, there was no clear evidence that arthralgias were due to arthritis, the psychotic episode was associated with a severe neurological involvement, and the anemia was not hemolytic. Thus, none of these three findings should be considered as diagnostic criteria of SLE according to the ACR.⁶ In addition, the ds-DNA was only mildly positive and was combined with consistent negative antinuclear and anti-ENA antibodies, and also normal complement levels. Some studies claim that ANA-negative Lupus in the Hep-2 cell era is exceptionally rare.⁷ Other diagnostic criteria for SLE have been suggested⁸ although they are less commonly applied.

A post-streptococcal disorder was considered as a diagnosis of exclusion and was based on the past medical history of recurrent amigdalitis with increased ASO titers, the onset of parkinsonism 2 weeks after a pharyngitis and the highly increased ASO titers related to the neurological deterioration. This diagnosis was further supported by the clinical, laboratory and imaging findings.

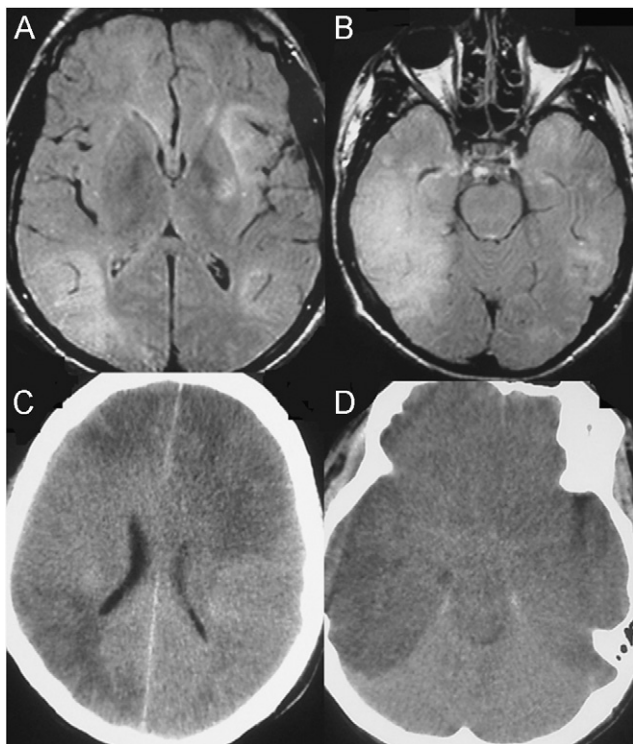


Fig. 1 – (A and B) Fluid-attenuated inversion-recovery (FLAIR) images performed on day 5 show bilateral cortico-subcortical high signal intensity lesions, with right predominance. The left insula and putamen are involved. (C and D) Brain CT performed on day 32 reveals extensive bilateral hypodensity, and brain edema, with effacement of the basal cisterns and surface sulci.

Although rarely, parkinsonism may be the unique manifestation of a post-streptococcal disorder.⁹ Moreover, the final clinical, laboratory and imaging findings in our patient parallel the encephalitis lethargica syndrome which is proved to be related to basal ganglia autoimmunity.¹⁰ Accordingly, the clinical picture that was seen consisted of somnolence, lethargy, parkinsonism and mutism. The CSF showed hyperproteinorrachia and lymphocytic pleocytosis and the MRI revealed high signal lesions on T2 involving the basal ganglia and other cortico-subcortical areas. Although it is currently hypothesized that an autoimmune process is the underlying pathophysiological mechanism in post-streptococcal disorders, specific disease related brain autoantigens have not been identified.¹¹ Thus, anti-basal antibodies should not be used yet for diagnostic purposes.¹² Our patient fits the original description of von Economo Encephalitis. Actually, the clinical onset may well correspond to the less common “amyostatic-akinetic” form and the last clinical picture to the “somnolent-ophthalmoplegic” form of this disease. Also, the clinical evolution seen in this patient is in accordance with the knowledge of von Economo. He wrote in 1929 that a recurrence of this disease would result in the somnolent-ophthalmoplegic form, which was frequently fatal.¹³ In the literature we have found only two patients^{9,10} presenting parkinsonism as a manifestation of a post-streptococcal disorder but a relapse to an encephalitis lethargica syndrome was not yet described.

In summary, the peculiarity of this case is the presentation by discrete parkinsonian syndrome, which was followed by an acute and catastrophic phase of a lethargic encephalitic syndrome, possibly precipitated by a new streptococcus infection and facilitated by the suspension of corticoids. This represents a new severe phenotype that should be added to the spectrum of post-streptococcal disorders, an etiology that should be considered in a movement disorder with a rapid detrimental evolution.

REFERENCES

1. Church AJ, Cardoso F, Dale RC, Lees AJ, Thompson EJ, Giovannoni G. Anti-basal ganglia antibodies in acute and persistent Sydenham's chorea. *Neurology* 2002;**59**:227–31.
2. Tucker LB, Menon S, Schaller JG, Isenberg DA. Adult- and childhood-onset systemic lupus erythematosus: a comparison of onset, clinical features, serology, and outcome. *Br J Rheumatol* 1995;**34**:866–72.
3. Font J, Cervera R, Espinosa G, Pallares L, Ramos-Casals M, Jimenez S, et al. Systemic lupus erythematosus (SLE) in childhood: analysis of clinical and immunological findings in 34 patients and comparison with SLE characteristics in adults. *Ann Rheum Dis* 1998;**57**:456–9.
4. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum* 1999;**42**:599–608.
5. Garcia-Moreno JM, Chacon J. Juvenile parkinsonism as a manifestation of systemic lupus erythematosus: case report and review of the literature. *Mov Disord* 2002;**17**:1329–35.
6. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;**25**:1271–7.
7. Kavanaugh A, Tomar R, Reveille J, Solomon DH, Homburger HA. Guidelines for clinical use of the antinuclear antibody test and tests for specific autoantibodies to nuclear antigens. American College of Pathologists. *Arch Pathol Lab Med* 2000;**124**:71–81.
8. Costenbader KH, Karlson EW, Mandl LA. Defining lupus cases for clinical studies: the Boston weighted criteria for the classification of systemic lupus erythematosus. *J Rheumatol* 2002;**29**:2545–50.
9. McKee DH, Sussman JD. Case report: severe acute Parkinsonism associated with streptococcal infection and antibasal ganglia antibodies. *Mov Disord* 2005;**20**:1661–3.
10. Dale RC, Church AJ, Surtees RA, Lees AJ, Adcock JE, Harding B, et al. Encephalitis lethargica syndrome: 20 new cases and evidence of basal ganglia autoimmunity. *Brain* 2004;**127**:21–33.
11. Church AJ, Dale RC, Giovannoni G. Anti-basal ganglia antibodies: a possible diagnostic utility in idiopathic movement disorders? *Arch Dis Child* 2004;**89**:611–4.
12. Singer HS, Hong JJ, Rippel CA, Pardo CA. The need for caution in considering the diagnostic utility of antibasal ganglia antibodies in movement disorders. *Arch Dis Child* 2004;**89**:595–7.
13. Dickman MS. von Economo encephalitis. *Arch Neurol* 2001;**58**:1696–8.